Listing of Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1-3. (Canceled)

4. (Currently Amended) A method of treating a patient suffering from diabetic cardiomyopathy, comprising administering ~~a therapeutically~~ an effective amount of ~~a GLP-1 molecule~~ a compound selected from the group consisting of Glucagon-Like Peptide-1 (GLP-1), GLP-1 analogs, and GLP-1-like peptides, to a patient suffering from diabetic cardiomyopathy.

5. (Currently Amended) The method ~~according to any one of~~ of claim ~~claims 1 through~~ 4, wherein the administration is continuous.

6. (Currently Amended) The method ~~according to any one of~~ of claim ~~claims 1 through~~ 4, wherein the administration is parenteral.

7. (Currently Amended) The method ~~according to any one of~~ of claim ~~claims 1 through 4~~, wherein said effective amount of ~~GLP-1~~ said compound is effective to cause a reduction in the plasma or heart norepinepherine level.

8-9. (Canceled)

10. (Currently Amended) The method of claim 6, ~~whereby the GLP-1 molecule~~ wherein said compound is administered in a dose of from about 0.1-10 pmol/kg/min.

11. (Currently Amended) The method of claim 4 ~~whereby the GLP-1 molecule~~ wherein said compound is administered subcutaneously in a dose of ~~from~~ about 0.5-50 pmol/kg/min.

12. (Currently Amended) The method of claim 4 ~~whereby the GLP-1 molecule~~ wherein said compound is administered in a dose of up to 10.0 nmol/kg.

13. (Canceled)

14. (Currently Amended) The method of claim ~~13~~ 4 ~~whereby the GLP-1 molecule~~ wherein said compound is administered intravenously in a dose of ~~from~~ about 0.1-10 pmol/kg/min.

15-16. (Canceled)

17. (New) The method of claim 4, wherein said compound is selected from the group consisting of GLP-1(1-37), GLP-1(1-36)NH_2, GLP-1(7-37), and GLP-1(7-36)NH_2.

18. (New) The method of claim 4, wherein said compound is a GLP-1 analog, and the Ala at position 8 of said GLP-1 analog is substituted with an amino acid selected from the group consisting of Ser and Thr.

19. (New) The method of claim 4, wherein said compound is a GLP-1 analog, and the Glu at position 9 of said GLP-1 analog is substituted with Asp.

20. (New) A method of treating a patient suffering from diabetic cardiomyopathy, comprising administering a therapeutically effective amount of an exendin.

21. (New) The method of claim 20, wherein the administration is continuous.

22. (New) The method of claim 20, wherein the administration is parenteral.

23. (New) The method of claim 20, wherein said effective amount of the exendin is effective to cause a reduction in the plasma or heart norepinepherine level.

24. (New) The method of claim 20, wherein said exendin is exendin-3.

25. (New) The method of claim 20, wherein said exendin is exendin-4.

26. (New) A method of treating a patient suffering from diabetic cardiomyopathy, comprising administering an effective amount of a compound which activates a receptor for glucagon-like peptide-1 (GLP-1).

27. (New) The method of claim 26, wherein the administration is continuous.

28. (New) The method of claim 26, wherein the administration is parenteral.

29. (New) The method of claim 28, wherein the compound is administered in a dose of from about 0.1-10 pmol/kg/min.

30. (New) The method of claim 26, wherein said effective amount of said compound is effective to cause a reduction in the plasma or heart norepinepherine level.

31. (New) The method of claim 26, wherein said compound is administered subcutaneously in a dose of from about 0.5-50 pmol/kg/min.

32. (New) The method of claim 26, wherein said compound is administered in a dose of up to 10.0 nmol/kg.

33. (New) The method of claim 26, wherein said compound is administered intravenously in a dose of from about 0.1-10 pmol/kg/min.

34. (New) The method of claim 26, wherein said compound which activates a receptor for GLP-1 is an exendin

35. (New) The method of claim 34, wherein said exendin is exendin-3.

36. (New) The method of claim 34, wherein said exendin is exendin-4

37. (New) The method of claim 26, wherein said compound which activates a receptor for GLP-1 is selected from the group consisting of GLP-1, GLP-1 analogs, and GLP-1-like peptides.

38. (New) The method of claim 37, wherein said compound is a GLP-1 analog, and the Ala at position 8 of said GLP-1 analog is substituted with an amino acid selected from the group consisting of Ser and Thr.

39. (New) The method of claim 37, wherein said compound is a GLP-1 analog, and the Glu at position 9 of said GLP-1 analog is substituted with Asp.

40. (New) The method of claim 37, wherein said compound which activates a receptor for GLP-1 is selected from the group consisting of GLP-1(1-37), GLP-1(1-36)NH_2, GLP-1(7-37), and GLP-1(7-36)NH_2.

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the above-identified application is respectfully requested. By the present amendment, the claims have been amended to remove multiple dependencies and to more clearly claim the invention. Furthermore, new claims 17-40 have been added. Claims 17-40 find support, at the very least, in the claims as originally filed, and on page 4, lines 5-6; page 12, line 1, to page 13, line 4; and page 14, lines 21-28, of the specification as filed. No new matter enters by this amendment.

In response to the Official Action mailed on March 11, 2003, Applicants provide the following remarks.

Rejection of Claims 4-7 and 9-16 Under 35 U.S.C. § 103(a)

Claims 4-7 and 9-16 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Aspnes *et al.* (USP 6,441,015) or Du Bois (USP 6,399,601) in view of Horikawa *et al.* (USP 6,235,481). For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

The Examiner's reliance on an argument that GLP-1, insulin and other treatments have been known to prevent diabetic cardiomyopathy is misplaced. Assuming that GLP-1 was known previously to treat diabetes, such a fact does not imply that GLP-1 would be useful for treating or preventing complications associated with diabetes such as diabetic cardiomyopathy.[1] Such complications, while perhaps exacerbated by hyperglycemia, are distinct medical conditions, and require medical treatment beyond that suitable for the treatment of hyperglycemia.

As noted in the specification on page 3, subjects suffering from diabetes often develop abnormal activation of the sympathetic nervous system. This abnormal activation results in increased levels of norepinepherine and its oxidative breakdown products, which can cause the

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[1] On page 6 of the Remarks section which accompanied the December 3, 2002, paper, it was stated that "[w]hile GLP-1, insulin, and other treatments used to maintain diabetics' insulin levels have been known to prevent diabetic cardiomyopathy..." (emphasis in the original). However, to be accurate, GLP-1, while it could be argued to have been known to be useful for treating diabetes, it was not known to prevent diabetic cardiomyopathy. As such, the

myocardial damage associated with diabetic cardiomyopathy. Existing treatments for diabetes will not necessarily reduce the levels of norepinepherine, and its oxidative breakdown products, and thus will not necessarily be useful for treating diabetic cardiomyopathy. Although insulin and other drugs for treating diabetes have been widely available for a long time, even as recently as late 2001 there still remained a need to develop approaches for the prevention and treatment of diabetic cardiomyopathy. *See* Cai *et al.*, "Oxidative stress and diabetic cardiomyopathy: a brief review," *Cardiovasc. Toxicol. 1(3)*:181-193 (2001) (attached hereto), in which this need for treatments for diabetic cardiomyopathy is discussed. Based on this continuing need in the area, it can be concluded that drugs useful in treating diabetes are not necessarily useful in the prevention of hyperglycemia-induced oxidative myocardial injury and the development of diabetic cardiomyopathy, much less in the treatment of diabetic cardiomyopathy once it has developed.

According to the Examiner, Aspnes *et al.* discusses the use of compositions comprising tetrazole compounds for treating a variety of conditions, including diabetes. The Examiner purports that the compositions of Aspnes *et al.* may further comprise, in addition to their tetrazole compound, another agent, such as GLP-1(7-37) and GLP-1(7-36)-NH_2. As noted above, drugs useful for treating diabetes are not necessarily useful for treating or preventing diabetic cardiomyopathy. Therefore, one of skill in the art would not assume that GLP-1 molecules, while purportedly useful in a composition for treating diabetes, would be also useful for treating diabetic cardiomyopathy.

The Examiner purports that Du Bois discloses compositions for treating a variety of conditions, including diabetes, comprising bicyclic pyrrolyl amides. Again, as with Aspnes *et al.*, the Examiner purports that the compositions may further comprise another agent, such as GLP-1(7-37) or GLP-1(7-36)-NH_2. However, as with Aspnes *et al.*, one of skill in the art would not assume that the GLP-1 molecules, while purportedly useful together with bicyclic-pyrrolyl amides in a composition for treating diabetes, would also be useful for treating diabetic cardiomyopathy.

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use of a compound to treat diabetes would not imply that such a compound would be useful for treating or preventing complications associated with diabetes.

The Examiner purports that Horikawa *et al.* discloses conditions associated with diabetes, including cardiomyopathy. However, there is no disclosure or suggestion that GLP-1 can be used for treating diabetic cardiomyopathy.

None of these references, either alone or taken together, disclose or suggest a method of treating a patient suffering from diabetic cardiomyopathy, comprising administering a therapeutically effective amount of GLP-1, GLP-1 analogs, GLP-1-like peptides, exendins, or a compound which activates a receptor for GLP-1. Not all therapies useful for treating diabetes would necessarily treat conditions associated with diabetes, such as diabetic cardiomyopathy, once they have occurred. *See*, again, the Cai *et al.* article, in which it is made clear that treatments for diabetic cardiomyopathy are needed (despite the advances in the discovery of treatments for diabetes). Therefore, it would not be obvious to one of skill in the art, from reading Aspnes *et al.*, Du Bois, and Horikawa *et al.*, that one could treat diabetic cardiomyopathy using GLP-1.

In light of these remarks, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

Rejection of Claims 4-7 and 9-16 Under 35 U.S.C. § 103(a)

Claims 4-7 and 9-16 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Efendic (USP 6,277,819) in view of Horikawa *et al.* For at least the reasons set forth below, withdrawal of this rejection is believed to be in order.

The Examiner purports that Efendic discloses treating diabetes with GLP-1, specifically GLP-1(7-36). However, as noted above, drugs useful for treating diabetes are not necessarily useful for treating or preventing diabetic cardiomyopathy. Therefore, one of skill in the art would not assume that GLP-1, while purportedly useful for treating diabetes, would be also useful for treating diabetic cardiomyopathy.

The Examiner purports that Horikawa *et al.* discloses conditions associated with diabetes, including cardiomyopathy. However, there is no disclosure or suggestion that GLP-1 can be used for treating diabetic cardiomyopathy.

Neither of these references, either alone or taken together, disclose or suggest a method of treating a patient suffering from diabetic cardiomyopathy, comprising administering a therapeutically effective amount of GLP-1, GLP-1 analogs, GLP-1-like peptides, exendins, or a compound which activates a receptor for GLP-1. Not all therapies useful for treating diabetes would necessarily treat conditions associated with diabetes, such as diabetic cardiomyopathy, once they have occurred. *See*, again, the Cai *et al.* article, in which it is made clear that treatments for diabetic cardiomyopathy are needed (despite the advances in the discovery of treatments for diabetes). Therefore, it would not be obvious to one of skill in the art, from reading Efendic and Horikawa *et al.*, that GLP-1 would be useful in a method for treating diabetic cardiomyopathy.

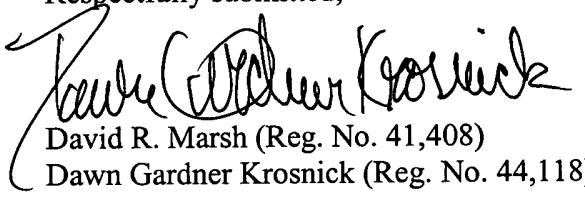
In light of these remarks, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,



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